PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
21475		
International Application No.	International Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/AU2003/000266	3 March 2003	1 March 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] G01N 33/15, 33/92; A61K 35/12, 45/06; C12Q 01/00; A61P 29/00

Applicant

WOMEN'S AND CHILDREN'S HOSPITAL et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of the report
29 September 2003	22 June 2004
Name and mailing address of the IPEA/AU	Authorized Officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	**JULIE GALE** Telephone No. (02) 6283 2272

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/000266

Basis of the report

With regard to the **elements** of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/000266

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be nonobvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☐ claims Nos:

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim Nos. **16-31**

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

The International Searching Authority found that there were multiple inventions and restricted the search to the invention as claimed in claims 1-15.

The claims of the Application are not linked by a special technical feature which is common to all independent claims nor is there evidence that the claims relate to the same inventive concept. A technical relationship (as defined in PCT Rule 13.2) does not exist.

The following inventions were found to exist:

1. Claims 1-15 relate to assays for grading a substance so as to assess its anti-inflammatory activity. The assay can be either an *in vivo* screening assay or an *in vitro* screening assay. The assay as a whole can be regarded as representing a **first "special technical feature"**.

2. Claims 16-20 relate to a pharmaceutical composition comprising emu oil or a biologically active extract or component thereof. As emu oil is well known, there is no "special technical feature" in claim 16 which could distinguish the composition from the prior art.

Claims 21-25 relate to a method of treating or ameliorating the symptoms of a T-cell mediated disease or a neutrophil mediated disease in a mammal by administering emu oil. Claims 30 and 31 relate to the preparation of emu oil by heating the oil to a temperature of at least 40°C. **A second "special technical feature"** can be regarded as the preparation of emu oil for therapeutic use and a method of therapeutic use of emu oil.

3. Claims 26-29 relate to the use of an organic solvent to extract compounds having anti-inflammatory activity from a biologically active oil or fat wherein the organic solvent may be an alcohol. This represents a **third "special technical feature"**.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. **1-15**

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **9-13, 15**	**YES**
	Claims **1-8, 14**	**NO**
Inventive step (IS)	Claims	**YES**
	Claims **1-15**	**NO**
Industrial applicability (IA)	Claims **1-15**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

The International Searching Authority raised the issue of a lack of unity. The Applicant declined to pay additional fees. As no International Search is available for claims 16-31, no meaningful opinion can be given.

Therefore only claims 1-15 are the subject of this International Preliminary Examination.

Claims 1-15 relate to either an *in vivo* or an *in vitro* assay system for grading a substance to assess, in a standardized manner, its anti-inflammatory activity.

The following documents were regarded as relevant in the ISR:

D1: Winter CA et al. (1962)

D2: Snowden JM and Whitehouse MW (1997)

D3: Hart PH et al. (2000)

D4: Lopez A et al. (1999)

D5: Whitehouse MW et al. (1998)

D6: Asuzu IU et al. (1999)

D7: WO 92/08470

D8: US 6,346,278

The relevance of each of these documents will be discussed with regard to the novelty of claims 1-15 below:

D1: This document discloses the carrageenin-induced edema in the hind paw of the rat as an assay for antiinflammatory drugs. The drugs are administered by gastric gavage an hour prior to injection of carrageenin in the foot. Swelling was then measured. This citation anticipates claims 1, 6-8 and 14 for novelty.

D2: This document discloses the study of the antiinflammatory activities of 5 different preparations of emu oil. M. tuberculosis in squaline as adjuvant was injected into the tail base of rats. Mixtures of emu oil/olive oil/cineole were applied topically to the ear. Rear paw diameters (swelling) were measured. Dose-response was then assessed. Ibuprofen, a well known anti-inflammatory, was tested. This document anticipates claims 1, 3-6, 8 and 14 of the current application.

D3: This document discloses the evaluation of potential anti-inflammatory properties of tea tree oil by examining the ability of tea tree oil to reduce the production in vitro of TNFα, IL-1β, IL-8, IL-10 and PGE_2 by LPS-stimulated human peripheral blood monocytes. These cells were used as a model for tissue macrophages. This document anticipates claims 2, 3, 4 and 14.

Supplemental Box
To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

D4: This document reports that topically applied emu oil reduces the severity of acute auricular inflammation induced by croton oil in mice. Both croton oil (as antigen) and emu oil were applied topically. Swelling was reduced with emu oil treatment. This document anticipates claims 1, 3-6, 8 and 14.

D5: This document discloses the measurement of paw swelling during the study of the anti-inflammatory properties of emu oil. It indicates that emu oil has trans-dermal anti-inflammatory activity. Other oils were tested including flax/linseed and evening primrose. This document anticipates claims 1, 3-6 and 8.

D6: This document discloses the application of croton oil (as antigen) to the surface of the ear to induce inflammation. Test substances were applied. The anti-inflammatory response was evaluated as percentage edema reduction. Also disclosed is an assay involving carrageenan-induced paw edema in rats. This citation anticipates claims 1, 3-8 and 14.

D7: This document discloses an anti-inflammatory composition derived from emu oil. Emu oil is administered topically, systemically and orally. There is a disclosure (see in particular Table 1 page 17) of rat oedema induced by tail base injection of M. tuberculosis in squaline followed by the topical application of oil and measurement of rear paw swelling. This document anticipates claims 1, 3-6 and 8.

D8: This document relates to the anti-inflammatory activity of a lipid-extract of mussels. Various modes of administration are discussed. Both an anti-inflammatory assay and an anti-arthritic assay are disclosed. This document anticipates claims 1, 3-8.

Observations on INVENTIVE STEP: Claims 1-15

In addition to the lack of novelty and inventiveness for claims 1-8 and 14, 15, the following observations are made on claims 3-5, 7, 14 and 15 in regard to the documents D1-D8.

D1: Claims 3-5 and 15 are objected to as lacking an inventive step as the features defined in these claims are considered in light of the common general knowledge as mere alternatives or choices for a person skilled in the art and are therefore not inventive.

D2: Claims 7 and 15 are not considered to be inventive for similar reasons as above.

D3: Claims 5, 9-13 and 15 are not considered to be inventive for similar reasons as above.

D4: Claims 7 and 15 are not considered to be inventive for similar reasons as above.

D5: Claims 7, 14 and 15 are not considered to be inventive for similar reasons as above.

D6: Claim 15 is not considered to be inventive for similar reasons as above.

D7: Claims 7, 14 and 15 are not considered to be inventive for similar reasons as above.

D8: Claims 5, 14 and 15 are not considered to be inventive for similar reasons as above.

Further to the above observations on inventive step above, claim 2 and appended claims are not considered to be inventive in view of the problem to be solved and the common general knowledge in this particular art.

The Applicant has disclosed an assay for the measurement of anti-inflammatory effects of substances. Therefore, the problem may be viewed as providing a means for assessing the anti-inflammatory activity of a substance.

The Applicant has demonstrated that an *in vitro* assay can be used to assess the anti-inflammatory activity of a substance wherein the test substance is added to an *in vitro* preparation of T-cells, macrophages or neutrophils. The activity of such cells is then observed and compared to the activity observed for a standard compound.

It is to be first noted that the comparison of a test substance against a known substance is standard practise in assays. For example, a standard curve may be generated and the activity of a test substance is then compared. Thus part (iv) of claim 2 cannot be considered to contribute an inventive step.

Supplemental Box
To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V: Inventive Step Observations

The person skilled in the art in relation to this current application would be someone with experience/knowledge of assay methodologies and would have an understanding of the inflammation process.

The use of cell culture as a means for assaying is well known and there are many examples of its use in the art (such as for toxicity testing of substances, monitoring the effects of test substances etc...). With particular attention to investigations of anti-inflammatory properties, it appears to be well known in the art to utilise certain cells which are known to be involved in the process of inflammation. Such cells involved in the anti-inflammatory process include macrophages, T-cells and neutrophils. For example, the literature regarding investigations of anti-inflammatory properties appears to be replete with disclosures concerning (a) the adhesion of neutrophils; (b) the use of LPS-induced macrophages and monitoring of TNF-α; (c) T lymphocyte proliferation *in vitro;* (d) chemotaxis involving neutrophils.

Therefore a claim to an assay involving the measurement of activity of an *in vitro* preparation of T-cells, macrophages or neutrophils is not regarded as demonstrating an inventive step in light of the common general knowledge. It is well known that such cells as macrophages, T lymphocytes and neutrophils are involved in the inflammation process. To then utilise these cells *in vitro* for the observation of anti-inflammatory properties of test substances cannot be regarded as demonstrating any inventiveness over and above what appears to be common general knowledge in this particular art.

In light of the above comments, claims 9-13 are also not considered to demonstrate an inventive step. A person skilled in this particular art who is acknowledged to have some understanding of the inflammation process would, without recourse to inventive faculty, arrive at the solution as defined in these claims. As stated above, it would seem to be well known to observe the proliferation of T cells as it relates to inflammatory processes (claim 9). The production of cytokines by T cells in the inflammation process is also well known, hence observations on the production of certain cytokines as indicators of anti-inflammatory activity cannot be regarded as inventive (claims 10 and 11).

INDUSTRIAL APPLICABILITY: This can be acknowledges for claims 1-15.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
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I. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
US 2003/0031724	13/02/2003	16/05/2001	16/05/2001

This document discloses anti-inflammatory compositions including those derived from emu oil. Example 1 (page 6) includes disclosure of an assay utilising the application of croton oil followed by emu oil to the inner surface of the ear of a mouse. Auricular thickness (ie degree of swelling) was observed. This citation would have particular relevance with regard to anticipating claims 1 and 3-8.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*